Covert Dyskinesia Associated with Aripiprazole: A Case Report

Tardive dyskinesia (TD) is characterized by involuntary movement generally of tongue, lower face, and jaw. Chronic exposure to antipsychotic drugs may lead to the development of TD, which can be permanent and irreversible even after discontinuation of antipsychotics. The exact mechanism of TD is still unclear despite many hypotheses being proposed, with the most well-known hypothesis being hypersensitivity of dopamine receptor [1]. Aripiprazole is a second-generation (atypical) antipsychotic, acting as a potent 5-HT₂₅ antagonist as well as partial D₂ and 5-HT₁₅ agonists. Extrapyramidal side effects of aripiprazole are reported to be fewer than those of typical antipsychotics. Cases have been reported in which TD remitted after antipsychotics shifting to aripiprazole [2]. But the risk of aripiprazole-associated TD may be underestimated [3]. In this report, we present a case with newly-onset orolingual dyskinesia after discontinuation of aripiprazole.

Case Report

A 67-year-old woman patient has been diagnosed with delusional disorder at the age of 47 years. She was treated with amisulpride 400 mg/day for half a year before receiving aripiprazole due to development of tremor over her left leg. Aripiprazole 10 mg/day was prescribed on day one and increased to 15 mg/day on day 27 due to persistent delusions. But her left leg tremor was worsened. Therefore, the dose of aripiprazole was tapered off and discontinued on day 125 after the improved psychotic symptoms. However, orolingual dyskinesia was developed on day 183. She was referred to a neurology clinic, where biperiden 2 mg/day and cyproheptadine 8 mg/day were given on day 188. Amantadine was also given briefly from day 203 to day 215. Clonazepam 0.5 mg/day was prescribed on day 228. Due to the side effect of dry mouth, biperiden was tapered off and discontinued on day 289. Left leg tremor and orolingual dyskinesia were improved gradually.

Comment

Gardos et al. [4] classified antipsychotic-associated TD into three groups: TD, withdrawal dyskinesia, and covert dyskinesia. When dyskinesia develops after dose reduction or discontinuation of antipsychotics, withdrawal dyskinesia or covert dyskinesia needs to be considered. Withdrawal dyskinesia refers to a self-limited condition with improvement after 6–12 weeks, whereas covert dyskinesia indicates a hidden form of dyskinesia, which can be permanent, breaking through after dose reduction or discontinuation.

According to a previous review, the annual incidence of TD caused by typical antipsychotic is 5.5% and that by atypical antipsychotics is about 3.9% [5]. One study reported a prevalence of aripiprazole-associated TD being 3.4% [6]. However, a series of case reports suggested that aripiprazole-associated TD may be underestimated [3]. Despite the previously identified risk factors of TD including affective disorder, male gender, older age, and presence of EPS [7], factors related to aripiprazole-associated TD remain under-researched.

Our patient developed newly-onset orolingual dyskinesia on day 58 following aripiprazole discontinuation, and dyskinesia improved partially after 20-week follow-up. Therefore, covert dyskinesia should be considered. We did a literature review of withdrawal dyskinesia and covert dyskinesia associated with aripiprazole. Moseley et al. [8] presented a case of a patient with aripiprazole use (15 mg/day) with venlafaxine for depression treatment who experienced abnormal tongue movement two weeks after aripiprazole cessation. Dyskinesia was partially improved after treatment with tetrabenazine 50 mg/day over the next three months. Patra et al. [9] reported a depressive patient, who developed dyskinesia three weeks after discontinuing aripiprazole 20 mg/day. Tetrabenazine 10 mg/day was given. The dyskinesia was improved in the following four weeks. Mahgoub et al. [10] reported another depressive patient taking aripiprazole 15 mg/day, who developed involuntary repetitive lip-smacking and chewing 12 weeks after aripiprazole cessation. He was lost to follow-up but was seen eight months later, when he was taking haloperidol, and showed no perioral movement. Although it could not be sure regarding whether the disappearance of perioral movement happened following the administration of haloperidol, dyskinesia did emerge again within 24 h after haloperidol cessation. Such finding may be in accordance with the theory that covert dyskinesia being a dyskinesia-to-be which is suppressed by the concurrent use of antipsychotic agents.

Compared to these cases, our patient was obvious in having different psychopathology (persecutory delusion rather than depression). The interval between the emergence of TD and aripiprazole cessation was eight weeks, falling between that of the three patients mentioned above. We gave different treatment regimens (biperiden, cyproheptadine, amantadine, and clonazepam), and dyskinesia was improved partially.

Future research is warranted to further clarify the roles of those medications in the management of aripiprazole-associated covert dyskinesia. The case report of our patient presented here adds to the existing literature, suggesting that aripiprazole-associated covert TD may be underestimated. Thus, adequate monitoring of involuntary movements in individuals tapering aripiprazole may be warranted. (The institutional review board at the Far Eastern Memorial Hospital approved the case report for publication).

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Conflicts of Interest
There are no conflicts of interest.

References